

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
18 December 2003 (18.12.2003)

PCT

(10) International Publication Number
WO 2003/103601 A3

(51) International Patent Classification⁷: **A61K 38/00**, G01N 33/567, C07K 14/00, 16/00

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(21) International Application Number:

PCT/US2003/018046

(22) International Filing Date: 5 June 2003 (05.06.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/386,551	5 June 2002 (05.06.2002)	US
60/386,527	5 June 2002 (05.06.2002)	US
60/386,521	5 June 2002 (05.06.2002)	US
60/386,936	6 June 2002 (06.06.2002)	US
60/386,429	6 June 2002 (06.06.2002)	US
60/386,954	6 June 2002 (06.06.2002)	US
60/387,301	7 June 2002 (07.06.2002)	US

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(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

Published:

— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
23 September 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS OF DIAGNOSING & TREATING DIABETES AND INSULIN RESISTANCE

(57) Abstract: The present invention provides compositions and methods for diagnosing and treating diabetes and insulin resistance. In particular, the invention provides methods of identifying modulators of the polynucleotides or polypeptides of the invention and using those modulators to treat diabetes, as well as methods of diagnosing diabetes by measuring the levels of the polynucleotides or polypeptides of the invention in a patient.

WO 2003/103601 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/18046

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/00; G01N 33/567; C07K 14/00, 16/00
 US CL : 514/2; 435/7.21; 530/350, 387.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 U.S. : 514/2; 435/7.21; 530/350, 387.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 STN, EAST: search terms diabetes, frizzled, protease

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6,153,420 A (SHEPPARD) 28 November 2000 (28.11.2000), column 11, lines 3-15.	1-11, 16, 17, 19-28
X		12-15, 18
A	HOANG, B. et al. Primary Structure and Tissue Distribution of FRZB, a Novel Protein Related to Drosophila Frizzled, Suggest a Role in Skeletal Morphogenesis. J. Bio. Chem. 18 October 1996, Vol. 273, No. 42, pages 26131-26137, especially pages 26132-26133.	1-11, 16, 17, 19-28
X		12-15, 18

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

15 June 2004 (15.06.2004)

Date of mailing of the international search report

28 JUL 2004

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/18046

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claim Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claim Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claim Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-28 as they relate to SEQ ID NOS:2, 16, 20

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest



The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/18046

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-28 in part, drawn to methods and compositions pertaining to SEQ ID NO: 2.

Group II, claim(s) 1-28 in part, drawn to methods and compositions pertaining to SEQ ID NO: 6.

Group III, claim(s) 1-28 in part, drawn to methods and compositions pertaining to SEQ ID NO: 8.

Group IV, claim(s) 1-28 in part, drawn to methods and compositions pertaining to SEQ ID NO: 10.

Group V, claim(s) 1-28 in part, drawn to methods and compositions pertaining to SEQ ID NO: 16.

Group VI, claim(s) 1-28 in part, drawn to methods and compositions pertaining to SEQ ID NO: 20.

Group VII, claim(s) 1-28 in part, drawn to methods and compositions pertaining to SEQ ID NO: 22.

Group VIII, claim(s) 1-28 in part, drawn to methods and compositions pertaining to SEQ ID NO: 28.

Group IX, claim(s) 1-28 in part, drawn to methods and compositions pertaining to SEQ ID NO: 30.

Group X, claim(s) 1-28 in part, drawn to methods and compositions pertaining to SEQ ID NO: 34.

The inventions listed as Groups I-X do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The claimed molecules have no common structure or activity. The linking feature is their use in the treatment of diabetes. Since treatment of diabetes is known in the art (see Goodman and Gilman, The Pharmacological Basis of Therapeutics, sixth edition, 1980, pp. 1514-1517), this does not constitute a special technical feature.